

REMARKS

Claims 1-20 are all the claims pending in the application. Claims 2-3, 5-6, 8-9 and 11-12 have been amended for further clarity.

In addition, in response to the Examiner's objection to the abstract of the disclosure, Applicant has replaced the Abstract with a new Abstract.

Entry of the above amendments is respectfully requested.

I. Response to Objection of Claims 2-3, 5-6, 8-9 and 11-12

At page 2 of the Office Action, claims 2-3, 5-6, 8-9, and 11-12 are objected to because of informalities.

Basically, the Examiner asserts that the limitations where ligands or receptors are bound to porous adsorptive regions are repeated numerous times within each of the instant claims and request appropriate correction.

Without acquiescing to the merits of the objection, claims 2-3, 5-6, 8-9, and 11-12 have been amended by inserting --bound-- before the receptor or ligand which has been bound to one of the porous adsorptive regions and by deleting the phrase "each of which has been bound to one of the porous adsorptive regions of the biochemical analysis unit" for purposes of further clarity.

In view of the above, withdrawal of the foregoing objection is respectfully requested.

II. Response to Rejection of Claims 2-3, 5-6, 8-9 and 11-12 under 35 U.S.C. §112, second paragraph

At pages 3-6 of the Office Action, claims 2-3, 5-6, 8-9, and 11-12 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner asserts the following:

A. In claims 2-3 (line 8), 5-6 (line 3), 8-9 (line 12), and 11-12 (line 15) the phrase "forcibly causing" is vague and indefinite because the specification does not provide a definition for the term and it is unclear what force causes the receptor and ligand to flow.

Applicant respectfully traverses the rejection.

At page 17, lines 16-19, the specification discloses that the liquid is forcibly caused to flow such that the liquid flows across each of the porous adsorptive regions of the biochemical analysis unit. In addition, for example, at page 39, lines 14-24, the specification discloses that the flowing means 30 comprises a reaction liquid circulating pipe 31 and a pump 32, one end of the reaction liquid circulating pipe 31 is releasably fitted to the reaction liquid inlet 25 of the reaction vessel 20, and the reaction liquid is forcibly caused to flow within reaction vessel 20. Further, in Example 1, the labeled antibody liquid was fed into the reaction vessel, and the pump was driven for one minute to cause the antibody liquid to permeate through all parts of the adsorptive regions of the biochemical analysis unit. *See* page 48, line 22 to page 49, line 2.

In view of the above, the phrase "forcibly causing" is believed to be clear and definite. In addition, it is respectfully submitted that the phrase is defined in the specification, and that one of ordinary skill in the art would understand the meaning and scope of the claim.

B. In claims 2-3, line 8 of the claims, the phrase "a receptor or a ligand" is vague and indefinite. It is not clear whether the receptor and ligand in the instant phrase is the same

or different from the ligands and receptors recited in the preceding phrase "to which ligands or receptors have been bound" (lines 4-5).

It is respectfully submitted that, in the present invention, a receptor or ligand is bound to the porous adsorptive regions and a labeled receptor or ligand is caused to flow across each of the porous adsorptive regions and bind to a receptor or ligand bound to the porous adsorptive regions. Without acquiescing to the merits of the rejection and to expedite prosecution, claim 2 has been amended by inserting --bound-- before "ligands" and "receptors" in the phrase "to which ligands or receptors have been bound" for purposes of further clarity.

C. In claims 2-3, the phrases "the receptor or the ligand" (line 9), "the receptor or the ligand" (line 11), "the ligands or the receptors" (line 12), "the receptor or the ligand" (line 14), "one of the ligands" (line 15), "one of the receptors" (line 17), "detecting the receptor or the ligand" (line 20), and "at least one of the ligands or at least one of the receptors" (lines 21-22) are vague and confusing. It is not clear whether the receptor and ligand in the instant phrases refer to the receptor and ligand in line 8 or to the ligands and receptors in lines 4-5, or to both.

Without acquiescing to the merits of the rejection, claims 2-3 have been amended to more clearly distinguish between the various ligands and receptors of the present invention.

D. In claims 2-3 (line 22 or the claims), 5-6 (line 21 of the claims), 8-9 (line 24 of the claims), and 11-12 (line 31 of the claims) the term "utilization" is vague and indefinite.

Applicant respectfully traverses the rejection.

As noted above, in the present invention, a labeled receptor or a labeled ligand is caused to flow across each of the porous adsorptive regions and bind to a receptor or ligand

bound to the porous adsorptive regions. Then, a chemical luminescence substrate having wavelengths falling within the visible light wavelength range is brought into contact with the labeled receptor or ligand and the chemical luminescence produced is detected photoelectrically. *See e.g.,* page 35, lines 4-14 and page 44, lines 10-24.

Accordingly, it is respectfully submitted that claims 2 and 3 are clear and definite, and that one of ordinary skill in the art would understand the meaning and scope of the claims.

E. In claims 2-3, line 28, the phrase "bubble removing process" is vague and indefinite. The specification does not provide a definition for the term and it is unclear what type of process is used for removing bubbles.

Applicant respectfully traverse the rejection.

In the present invention, there is a risk that a gas, which is present in fine voids of the adsorptive regions of the biochemical analysis unit will form bubbles, and that bubbles will mix into the liquid at the time of change-over between the reaction liquid and the washing liquid. *See* page 40, lines 6-10. Therefore, a bubble removing process is employed in the present invention. *See e.g.,* page 40, lines 11-13. In the bubble removing process, for example, a net or filter, which is capable of catching the bubbles is used. *See* page 40, line 24 to page 41, line 1.

Accordingly, it is respectfully submitted that claims 2 and 3 are clear and definite, and that one of ordinary skill in the art would understand the meaning and scope of the claims.

F. In claims 8-9, lines 3-4, the phrase "subjecting the receptor or the ligand to the specific binding with the ligands or the receptors" is vague and confusing. The instant phrase suggests that there are two sets of either ligands or receptors and that the two sets perform

specific binding with each other. However, the parent claims 2-3 only recite one set of ligands or receptors (lines 4-5), and that the ligands or receptors are bound to the porous adsorptive regions. Therefore, it is confusing as to whether there are two sets of ligands or receptors, and in the case that there is only one set, how the ligands or receptors can perform specific binding if they are all immobilized onto a surface.

Without acquiescing to the merits of the rejection, claims 8 and 9 have been amended for purposes of further clarity in a manner similar to claims 2 and 3 to more clearly distinguish between the various ligands and receptors of the present invention.

G. In claims 8-9, the phrases "the receptor or the ligand" (line 6), "at least one of the ligands" (line 7), "at least one of the receptors" (line 9), "the receptor or the ligand" (lines 16-17), "the ligands" (line 18), "the receptors" (line 20), "the receptor or the ligand" (line 23), "one of the ligands" (line 24), and "one of the receptors" (line 25) are vague and indefinite. It is unclear whether the ligands and receptors in the instant phrases are the receptors and ligands of line 3 of the instant claims, or if they are the receptors and ligands of line 4 of the instant claims.

Without acquiescing to the merits of the rejection, claims 8 and 9 have been amended for purposes of further clarity in a manner similar to claims 2 and 3 to more clearly distinguish between the various ligands and receptors of the present invention.

H. In claims 11-12, lines 3-5, the phrase "auxiliary substance-bound receptor or an auxiliary substance-bound ligand, to which an auxiliary substance has been bound" is vague and confusing. The terms "auxiliary substance-bound receptor" and "auxiliary substance-bound ligand" indicate that the receptors and ligand are already bound to auxiliary substances.

Therefore, it is unclear whether the term "auxiliary substance" in lines 4-5 refers to the auxiliary substances already bound to the receptors and ligands, or whether it is another auxiliary substance different from the ones bound to the receptors and ligands.

Without acquiescing to the merits of the rejection and to expedite prosecution, claims 11-12 have been amended to delete the phrase "to which an auxiliary substance has been bound" since it is clear from the use of the phrase "auxiliary substance-bound receptor or an auxiliary substance-bound ligand" that the auxiliary substance is already bound to the receptor or ligand.

In view of the above, withdrawal of the §112 rejections is respectfully requested.

III. Response to Rejection of claims 2-3, 5-6, 8-9 and 11-12

At pages 6-8 of the Office Action, claims 2-3 and 5-6 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Besemer et al (US 6,140,044).

Applicant respectfully traverses the rejection.

In the present invention, the biochemical analysis unit is provided with a plurality of porous adsorptive regions to which ligands or receptors have been bound respectively. At page 19, line 21-35, the present specification discloses that the biochemical analysis unit comprises a base plate 2, which is provided with a plurality of holes and a plurality of adsorptive regions, each of which is filled in one of the holes. The holes in the base plate are made by, for example, punching with a pin, electrical discharge machining, etching or laser beam irradiation.

See page 24, lines 11-17. A labeled receptor or ligand is forcibly caused to flow such that the liquid flows across each of the porous adsorptive regions of the biochemical analysis unit. Basically, the fluid containing the labeled receptor or ligand forced to pass through the porous

adsorptive regions using a pump, thereby allowing the labeled receptor or ligand to bind specifically with the receptor or ligand bound to the porous adsorptive regions.

The present invention prevents the problem of bubbles being generated and clinging to the surfaces of the adsorptive regions when forcibly causing fluid to flow. The reason for the problem is that bubbles, which are present in the porous adsorptive region, are generated when fluids are forced to flow across porous adsorptive regions.

Besemer et al. relates to a device for packaging a substrate having an array of probes (i.e., a surface-immobilized molecule that is recognized by a particular target and sometimes referred to as a ligand) fabricated on its surface. In the bio array chip of Besemer et al., fluid may be forcibly caused to flow, but not so that the fluid flows across the bio array chip. Therefore, bubble generation is not a problem in the invention of Besemer et al. That is, the generation of bubbles is a problem that occurs when the two factors are present: (1) the portion to which a ligand or a receptor is bound is a porous adsorptive region, and (2) fluid is caused to flow across the porous adsorptive region. Besemer et al. do not disclose flowing a fluid across the adsorptive region as in the present invention, and thus, generation of bubbles is not a problem.

Hence, Besemer et al. do not teach the present invention.

In addition, the present invention and the invention of Besemer et al. differ for the following reasons. As the Examiner has pointed out, Besemer et al. teach that the removal of bubbles from the cavity is facilitated at column 8. However, this disclosure relates simply to bubbles which are included in the fluid introduced into the cavity. These bubbles can be removed simply by providing entrances to the cavity at the highest point and at the lowest

point thereof. However, bubbles that have passed through porous adsorptive regions and cling to the surfaces thereof are extremely small and cannot be removed in this manner.

Also, Besemer et al. disclose at column 8 that “[t]he bubbles agitate the fluid, increasing the hybridization rate between the targets and the complementary probe sequences” (col. 8, lines 8-10). From this disclosure, it is clear that the bubbles that are the problem to be solved by the present invention and the bubbles described in Besemer et al. are completely different in their formation processes and their very nature.

Further, at pages 9-11 of the Office Action, claims 8-9 and 11-12 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Besemer et al. in view of Bronstein et al (US 5,543,295).

Each of claims 8-9 and 11-12 depend directly from claims 2 or 3. Therefore, it is respectfully submitted that these claims are patentable over Besemer et al. for at least the same reasons as claims 2 and 3.

In addition, Bronstein relates to an improvement in chemical luminescence of dioxytane and does not make up for the deficiencies of Besemer et al. Further, as note above, the present invention is concerned with the removal of bubbles generated when a fluid is forcibly caused to flow across a porous adsorptive region. In view of the differences between the present invention and Besemer et al. and the fact that Besemer et al. are not concerned with bubbles generated when a fluid is forcibly caused to flow across a porous adsorptive region because Besemer et al. do not teach flowing a fluid across a porous adsorptive region, one of ordinary skill in the art would not arrive at the present invention based on the disclosure of

Besemer et al. and Bronstein. That is, even if Besemer et al. and Bronstein were somehow combined, the present invention would not be achieved.

In view of the foregoing, withdrawal of the §102 and 103 rejections is respectfully requested.

IV. Conclusion

In conclusion, reconsideration and withdrawal of the objections and §112, 102 and 103 rejections, and allowance of claims 2-3, 5-6, 8-9 and 11-12 are respectfully requested.

If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

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